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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,924	AMARA ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *1-54 and 62-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/4/05; 4/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Please direct all future correspondence to Examiner Stacy Chen of Art Unit 1648. Applicant's election of Group III, claims 56-61, is acknowledged and entered. Applicant did not indicate whether the election was made with or without traverse. Since Applicant has not presented any arguments as to the merits of the restriction, the election has been treated as an election without traverse. Claims 1-55 and 62-71 are withdrawn from consideration, being drawn to non-elected subject matter. Claims 56-61 are under examination.

Claim Objections

2. Claims 56-61 are objected to for a minor informality. In the method steps of claims 56 and 57, the cells are not specified as being dendritic cells, although the last paragraph of both claims indicates that dendritic cells are essential to the assay. The claims should refer to the cells as dendritic cells (DC) for consistency and avoiding a lack of antecedent basis. If Applicant amends the claims as suggested, claim 58 would be redundant. Correction is required.

Specification

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 56 recites "about 95% modulation of binding of the viral effector molecule to dendritic cells by the test substance". The specification discloses 95% inhibition in paragraph [0109], but not 95% modulation, which encompasses more than inhibition activity. Correction is required.

Claims Summary

4. The claims are drawn to a method of identifying a DC-SIGN modulator, or more specifically, a DC-SIGN blocker. (DC-SIGN is a DC-specific adhesion receptor, also called ICAM-grabbing non integrin and CD-209. DC-SIGN is the ligand of ICAM-3, see specification page 5, paragraph [013]). The specification defines "DC-SIGN receptor" as DC-SIGN, DC-SIGNR (DC-SIGN related protein), or homologues thereof [page 17, paragraph [057]). The method steps comprise the determination of a test substance binding inhibition value. This value is determined by dividing a test substance binding value by a baseline binding value.

Test substance binding inhibition value = test substance binding value / baseline binding value

The *test substance binding value* is determined by exposing cultured cells comprising a DC-SIGN receptor to a marked viral effector molecule binding moiety in the presence of a test substance, and allowing binding equilibrium to be reached. The extent of binding is the test substance binding value. The *baseline binding value* is determined by exposing cultured cells comprising a DC-SIGN receptor to a marked viral effector molecule binding moiety and allowing binding equilibrium to be reached. The extent of binding is the baseline binding value. If the test substance binding inhibition value represents an about 95% modulation or inhibition of binding of the viral effector molecule to dendritic cells by a test substance, the test substance is deemed a substance that substantially modulates or inhibits the binding of a viral effector molecule to the DC-SIGN receptor.

Specifically, the cells are dendritic cells (DC) or human acute monocytic leukemia cells (THP-1, ATCC TIB 202). The viral effector molecule is Dengue virus E glycoprotein.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- All claims refer to binding values for a baseline, a test substance, and a resultant test substance inhibitor value. The specification does not clearly set forth the units for measuring these binding values. The claims recite, "determining the extent of binding of the marked viral effector molecule binding moiety to the cultured cells to thereby determine a baseline binding value", however, it is not clear what exactly the value is to be measured with. Lacking a clear definition of the units for measurement of these binding values, the metes and bounds of the claims cannot be determined.
- All claims refer to "DC-SIGN receptor". As noted above, the specification defines "DC-SIGN receptor" in the human context, as DC-SIGN, DC-SIGNR (DC-SIGN related protein), or homologues thereof [page 17, paragraph [057]). The "DC-SIGN receptor" in the non-human animals refers to homologues of a human DC-SIGN receptor (page 17, paragraph [058]. While the identity of DC-SIGN and DC-SIGNR is recognized in the art, the homologues of DC-SIGN and DC-SIGNR are not clearly defined in the specification. Homologues broadly encompass any protein having some degree of similarity (structurally or functionally) to DC-SIGN and DC-SIGNR. Further, according to paragraph [058], the receptor may be a homolog of a homolog. Applicant has not

defined the homologues' structures such that the metes and bounds of the homologues can be determined.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a DC-SIGN blocker, wherein the viral effector molecule is gE of Dengue virus and the DC-SIGN receptor is DC-SIGN (not homologues thereof), does not reasonably provide enablement for a method of identifying a DC-SIGN modulator, wherein the viral effector molecule is a non-gE of Dengue virus and the DC-SIGN receptor is a DC-SIGN homolog. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims encompass a method of identifying a DC-SIGN modulator that modulates the binding of a marked viral effector molecule to DC-SIGN. As discussed in the rejection under 35 U.S.C. 112, second paragraph above, the definition of DC-SIGN is not clear because it encompasses homologues of both DC-SIGN, DC-SIGNR and homologues of homologues.

The state of the art shows confirms that DC-SIGN mediates Dengue virus infection of human dendritic cells, specifically THP-1 cells, by binding envelope protein (Tassaneetrithep *et al.*, *The Journal of Experimental Medicine*, 2003, 197(7):823-829, see abstract and page 828, first column, filed in IDS of 5/4/05). The state of the art also confirms that DC-SIGN binds Human Cytomegalovirus (envelope protein B) and HIV gp120 (Kwon *et al.*, *Immunity*, 2002, 16(1):135-144, abstract, filed in IDS of 5/4/05, and Halary *et al.*, *Immunity*, 17(5):653-664, abstract, filed in IDS of 5/4/05).

The specification is specifically directed to a viral effector molecule of Dengue virus, the envelope glycoprotein (page 6, paragraph [016]). There are no other Dengue virus molecules identified in the specification as capable of interacting with DC-SIGN. Further, the specification does not provide guidance for identifying DC-SIGN and DC-SIGNR homologues, or homologues of homologues. There is insufficient information relating to the construction of homologues that would be useful in the claimed method.

Given the breadth of the claims, the state of the art, and the limited guidance and working examples in the specification, it would require undue experimentation to practice the claimed method in its full breadth.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Figdor *et al.* (WO 00/63251, "Figdor", filed in IDS of 5/4/05). The claims are summarized above. Figdor discloses the identification of a compound that binds to DC-SIGN on dendritic cells ("a C-type lectin") for modulating the interaction, particularly, reducing the interaction (see page 6, first and second full paragraphs). Figdor discloses the determination of antibodies that bind to DC-SIGN on dendritic cells, and the determination that those antibodies can reduce HIV infectivity of dendritic cells (see Example 8). Although the specific method steps of determining baseline values are not explicitly set forth in Figdor's disclosure, the basic steps are disclosed. Dendritic cells expressing DC-SIGN are pulsed with HIV-1 and infection is measured. Dendritic cells are also pulsed with anti-DC-SIGN antibodies prior to exposure to HIV-infected PBMCs, and infection is measured. A comparison between the two values is determined (see pages 28-29). It would have been well within the ability of the ordinary artisan to select a value (a percentage, for example) that represents significant modulation of DC-SIGN activity. Therefore, the claims are obvious over the disclosure of Figdor.

8. Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Figdor *et al.* (WO 00/63251, "Figdor", filed in IDS of 5/4/05) as applied to claim 57 above, and further in view of

Banka *et al.* (*Journal of Lipid Research*, 1991, 32:35-43, "Banka"). The claim is limited to THP-1 cells, which are human acute monocytic leukemia cells. Figdor does not disclose THP-1 dendritic cells, although Figdor does disclose the derivation of DCs from monocytes (see Example 1). It is well known in the art, evidenced by Figdor, that DCs are derived from monocytes. Given that Figdor uses cells that express DC-SIGN, and the THP-1 monocytic cell line is immortalized and produces immature DCs, it would have been obvious to select a cell line like THP-1 for an assay that requires continuous expression of DC-SIGN because the THP-1 cell line is expected to produce dendritic cells that express DC-SIGN. One would have had a reasonable expectation of success that the THP-1 cell line would have expressed DC-SIGN because it produces dendritic cells, which are known to express DC-SIGN.

Conclusion

9. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B Chen/

Primary Examiner, Art Unit 1648